

# Young Female COVID-19 Patient Presenting with Epileptic Seizure

## Epileptik Nöbetle Başvuran Genç Kadın COVID-19 Hastası

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### Abstract

COVID-19 is a new type of coronavirus infection with a wide clinical spectrum, ranging from asymptomatic to severely symptomatic, and that mostly affects the respiratory tract. Although the respiratory tract is the primary area affected by the disease, neurological symptoms such as headache, dizziness and muscle ache have also been reported in some patients since the early stages of the pandemic. COVID-19 symptoms and complications can affect the peripheral and central nervous systems as well as the skeletal muscles, while epileptic seizure is a rare manifestation of COVID-19. We present here the case of a female patient admitted to hospital with epileptic seizure due to COVID-19 encephalopathy.

**Key words:** COVID-19, seizures, encephalopathy.

### Öz

COVID-19, asemptomatikten şiddetli semptomlarla giden hastalığa kadar geniş bir klinik spektrum gösteren, çoğunlukla solunum yollarını etkileyen yeni tip koronavirüs enfeksiyonudur. Hastalıkta temel etkilenen bölge solunum sistemi olsa da, pandeminin erken evrelerinden itibaren bazı hastalarda, baş ağrısı, baş dönmesi ve kas ağrıları gibi nörolojik semptomlar da bildirilmiştir. COVID-19 semptomları ve komplikasyonları, hem periferik hem de santral sinir sistemini ve iskelet kaslarını etkileyebilir. Epileptik nöbet, COVID-19'un nadir bir belirtisidir. Biz de COVID-19 ensefalopatisi nedeniyle, hastaneye epileptik nöbet ile başvuran bir kadın hastayı sunuyoruz.

**Anahtar Sözcükler:** COVID-19, nöbet, ensefalopati.

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Coronavirus disease 2019 (COVID-19) is a new type of coronavirus infection that was first defined as an atypical pneumonia epidemic in the city of Wuhan, China in December 2019, and was later upgraded to a pandemic by the World Health Organization (WHO) on March 11, 2020. COVID-19 presents with a wide clinical spectrum that ranges from asymptomatic to severely symptomatic, and that mostly affects the respiratory tract (1). COVID-19 is caused by the recently identified severe acute respiratory distress syndrome coronavirus 2 (SARS-CoV-2), and is an ongoing global health emergency (2).

We present here a case who applied to the hospital emergency service with seizure that was treated as meningitis, but was later evaluated to be encephalopathy related to COVID-19.

## CASE

A 19-year-old female patient with no known disease referred to the emergency service with complaints of fever, fatigue and headache that did not respond to the antipyretics she used at home. An oropharyngeal swab for COVID-19 was subjected to a real-time Reverse Transcription-Polymerase Chain Reaction (RT-PCR) test and the patient's symptoms were treated, including metoprolol, and she was discharged. After experiencing dizziness at 03:00 on the same day, her speech gradually deteriorated and she became incomprehensible, and meaningless speech, empty gaze and disorientation developed. Tremors were noted in the right arm and leg, along with spasms in the left arm and leg, and balance disorder developed. She reappeared to the emergency department with these complaints, reporting no sleep disturbance, long-term hunger or head trauma before the seizure. The patient produced loud moans, meaningless sounds and empty gazes, while system examinations were normal. The patient's serum creatinine was 0.54 mg/dl, C-reactive protein (CRP) 3.3 mg/l (reference range: 0-5), white blood cell count 5.9 10<sup>9</sup>/L, lymphocyte 0.7 10<sup>9</sup>/L (12%), platelet 241 10<sup>9</sup>/L, hemoglobin 14.3 g/dl and d-dimer 1.33 mg/L (reference range: 0-0.55). No abnormal findings were detected on chest X-ray or thorax computed tomography (Figure 1), and the seizure was thus evaluated as an extrapyramidal side effect of metoprolol use. The patient was followed up in the general intensive care unit due to the continued confusion and contractions of extremities. A nasopharyngeal RT-PCR test for SARS-CoV-2 was positive and brain magnetic resonance imaging (MRI) produced normal findings. A lumbar puncture analysis revealed a protein level of 50.7 mg/dl in cere-

brospinal fluid (CSF). The CSF cell count was 14 $\mu$ L-10 mononuclear and 2 polymorphonuclear cells without red blood cells. Due to the fever, the high CRP of 68 mg/L and the white blood cell count of 11.4 10<sup>9</sup>/L, the patient was started on antiepileptic, favipiravir, ceftriaxone, levofloxacin and vancomycin treatments with an initial diagnosis of meningitis and COVID-19.

On the sixth day of hospitalization the patient was transferred to the inpatient service after her state of consciousness improved. She was able to make short sentences and to respond to single commands. On the second day of inpatient service follow-up, her seizures recurred, and she was returned to the intensive care unit as her oxygen saturation decreased to 88%. A further lumbar puncture was made on the ninth day of hospitalization: the CSF protein (15 mg/dl) and glucose (75 mg/dl) values were within the normal range; mycobacteria PCR and ARB (Acid Resistant Bacilli) in the CSF were negative. No mycobacteria or any other microorganisms were cultured from CSF. Brucella Coombs and Rose Bengal agglutination tests in the CSF were negative, and so the diagnosis of meningitis was excluded. The patient was in a state of confusion, but her comprehension and word output was intact. As lobar consolidation observed in the PA chest X-ray, taken on the 10th day of hospitalization, meropenem antibiotherapy was given for 14 days with a diagnosis of hospital-acquired pneumonia (Figure 2). On the 11th day of hospitalization, the patient was taken to the inpatient service for further follow-up as her general condition was improving and there had been no recurrence of seizures. Electroencephalography (EEG) taken on the 15th day was consistent with moderate encephalopathy (Figure 3a), and brain MRI taken on 19th day was normal. In the light of the patient's clinical, laboratory and radiological findings, her condition was evaluated as encephalopathy secondary to COVID-19. Levetiracetam was given from the beginning of admission to the hospital, and oxygen support with nasal cannula was given during hospitalization. The patient was discharged on the 23rd day of hospitalization due to the regression of infiltrations on chest X-ray, the improvement of oxygen saturation, the regression of acute phase reactants and the completion of antibiotic therapy (Figure 4). At discharge, CRP was <3 mg/l and white blood cell count was 7.82 10<sup>9</sup>/L. It was planned to proceed with levetiracetam treatment for 6 months due to the patient's history of seizures. When the patient applied for follow-up control examination 25 days after discharge, her complaints were dimin-

ished. The control EEG was consistent with mild encephalopathy (Figure 3b).

## DISCUSSION

COVID-19 is a pandemic disease that presents with clinical pictures ranging from mild illness with non-specific symptoms to respiratory failure with acute respiratory symptoms, and to severe pneumonia and sepsis (3). Epileptic seizure is a rare manifestation of COVID-19 (4). Coughs, fever, fatigue and shortness of breath are common symptoms of COVID-19, and many neurological abnormalities have been reported in patients with COVID-19 from the beginning of the pandemic. Among these, loss of smell and taste are distinctive symptoms that were later added to the clinical findings of the disease. The respiratory tract is the primary affected area in the disease, although neurological symptoms such as headache, dizziness and muscle ache have also been reported since the early stages of the pandemic. Neurological involvement in COVID-19 is a considerable component of the disease, as it has been reported that approximately 90% of patients with a diagnosis of COVID-19 have at least one subjective neurologic complaint (3). COVID-19 symptoms and complications can affect the peripheral and central nervous systems as well as skeletal muscles (2).

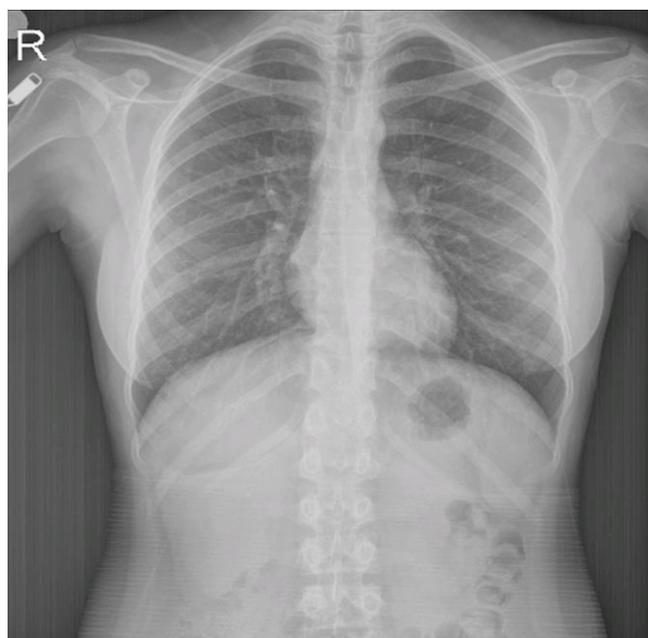


Figure 1: Chest X-ray upon presentation with no abnormal finding

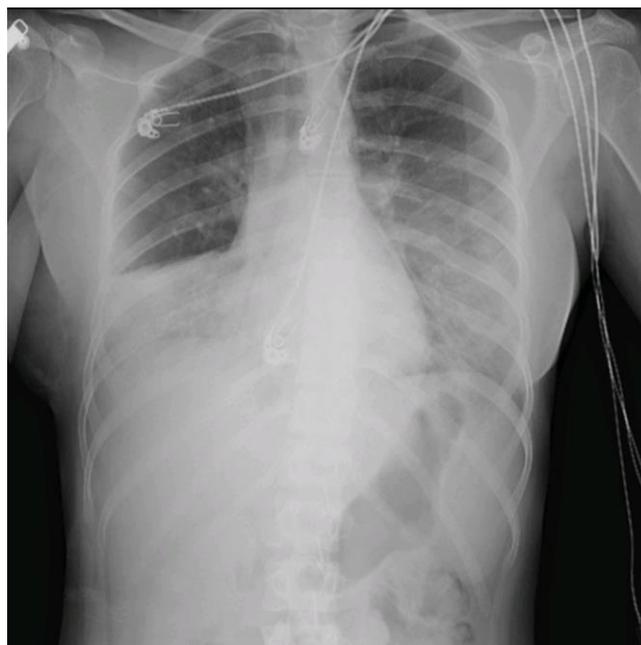
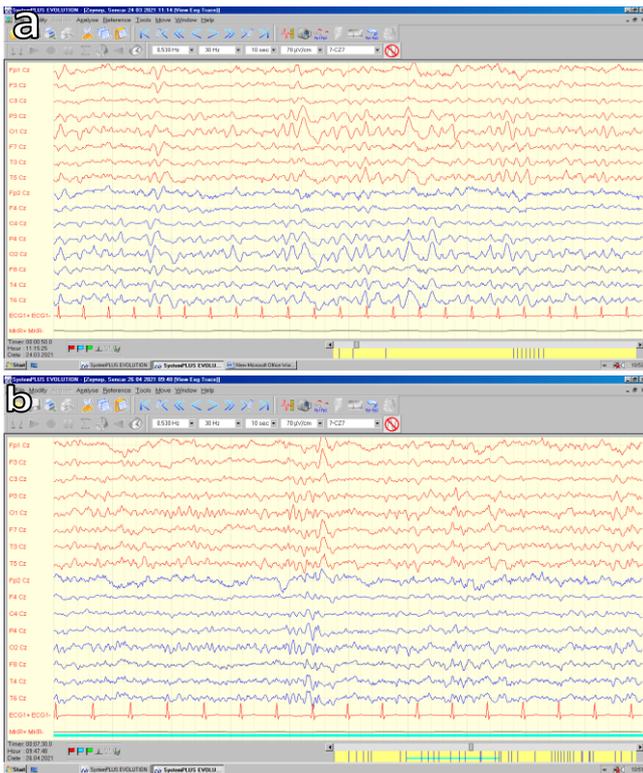


Figure 2: Lobar consolidation in the right lower zone of the lung

Viral neuroinvasion may occur via several routes, including transsynaptic transfer across infected neurons, entry via the olfactory nerve, infection of vascular endothelium or leukocyte migration across the blood-brain barrier (5). Neurological involvement in COVID-19 can present with many neurological manifestations, such as encephalopathy, encephalitis, ischemic stroke and postinfectious neurological complications (6).

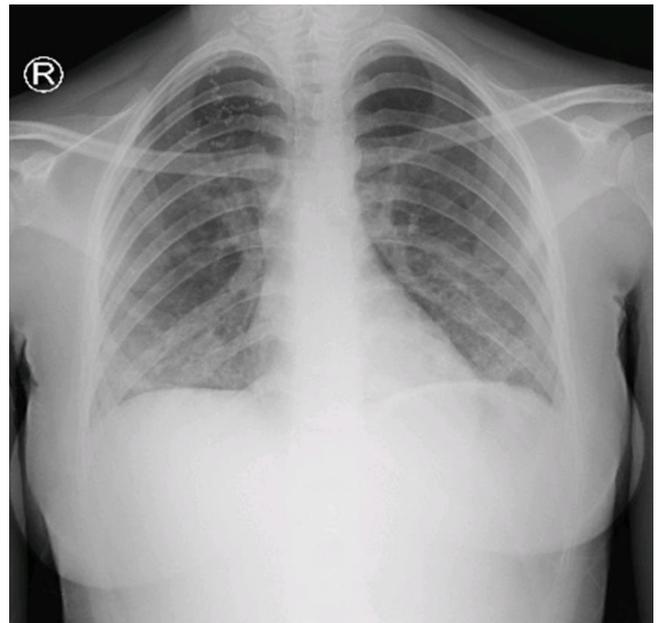
Neurological manifestations in SARS-CoV-2 infection due to encephalopathy/encephalitis and acute cerebrovascular disease have been observed in up to 8% of patients with severe disease (7). There have been a few cases of COVID-19 fulfilling the diagnostic criteria for infectious encephalitis (8,9), with the main findings in such cases being altered mental status, fever, seizures, white blood cells in CSF and focal brain abnormalities on neuroimaging. SARS-CoV-2 has been detected in the CSF in two patients (10,11), and temporal lobe encephalitis was confirmed by biopsy that showed perivascular lymphocytic infiltrates and hypoxic neuronal damage in one patient (8).

In the study by Meppiel et al. (12), 222 COVID-19 cases from 46 centers in France with neurological involvement were reviewed. COVID-19-associated encephalopathy was observed most commonly in 30% of the patients, followed by acute ischemic cerebrovascular disease in 25%, encephalitis in 9.5% and Guillian Barre Syndrome in 6.8%.



**Figure 3a and b:** Initial EEG showing delta and theta waves compatible with moderate encephalopathy (a), and follow-up EEG with theta waves compatible with mild encephalopathy (b)

COVID-19 patients may initially refer to clinics with headache, fever and new-onset seizure. In some COVID-19 patients, SARS-CoV-2 was found in the CSF, showing that this neurological manifestation can be attributed to the virus. However, COVID-19 patients presenting with acute meningoencephalitis with neither SARS-CoV-2 nor other viral pathogens detected in the CSF have also been seen. As such, SARS-CoV-2 RNA undetected in the CSF may indicate that direct brain infection is not the only means of neuroinvasion, and that other possible ways of transmission may exist, such as peri-infectious inflammation and altered neurotransmission, as underlying reasons for meningoencephalitis (2). Lymphocytic pleocytosis may be seen in the CSF of COVID-19 patients (13,14). Since meningoencephalitis can be complicated by intracerebral and subdural hematomas, early detection of the virus is essential to ensure the start of appropriate treatment and to prevent the onset of hemorrhagic encephalopathy, which can lead to severe disability or life-threatening situations (2).



**Figure 4** The regression of infiltrations on chest X-ray

Such neurological involvements as encephalopathy, cerebrovascular disease and Guillan Barre Syndrome can also complicate in the course of COVID-19 infection (1). Our patient presented with prominent neurological symptoms rather than respiratory symptoms, suggesting that COVID-19 infection should be kept in mind in patients presenting with epileptic seizure. Encephalopathy and encephalitis may develop during the hospitalization of COVID-19 patients who present initially with respiratory symptoms (15).

## CONCLUSION

Healthcare professionals should be aware that COVID-19 patients may develop encephalopathy at admission or during hospitalization, and so all appropriate examinations and investigations should be performed.

## CONFLICTS OF INTEREST

None declared.

## AUTHOR CONTRIBUTIONS

Concept - O.U., S.K., K.T., C.A.Y., S.B., N.C.; Planning and Design - S.K., O.U., K.T., C.A.Y., S.B., N.C.; Supervision - O.U., S.K., K.T., C.A.Y., S.B., N.C.; Funding - C.A.Y., S.B., N.C.; Materials - C.A.Y., S.B., N.C.; Data Collection and/or Processing - S.B., C.A.Y., N.C.; Analysis and/or Interpretation - K.T., S.K., O.U.; Literature Review - O.U., S.K.; Writing - K.T., S.K., O.U.; Critical Review - K.T., O.U., S.K.

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